(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 October 2004 (21.10.2004)

PCT

(10) International Publication Number
WO 2004/090135 A3

(51) International Patent Classification[7]: C12N 15/19, 15/62, C07K 14/52, 19/00, A61K 38/19, 39/395, C07K 16/00

(21) International Application Number: PCT/GB2004/001572

(22) International Filing Date: 7 April 2004 (07.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0308088.4	9 April 2003 (09.04.2003)	GB
0324235.1	16 October 2003 (16.10.2003)	GB

(71) Applicant *(for all designated States except US)*: **ASTERION LIMITED** [GB/GB]; Firth Court, Sheffield S10 2TN (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **ROSS, Richard** [GB/GB]; Asterion Limited, Firth Court, Sheffield S10 2TN (GB). **SAYERS, Jon** [GB/GB]; Asterion Limited, Firth Court, Sheffield S10 2TN (GB). **ARTYMIUK, Peter** [GB/GB]; Asterion Limited, Firth Court, Sheffield S10 2TN (GB).

(74) Agent: **HARRISON GODDARD FOOTE**; 31 St. Saviourgate, York YO1 8NQ (GB).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 28 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CYTOKINE POLYPEPTIDES AND ANTIBODIES CONTAINING A SIGNAL SEQUENCE FOR THE ATTACHEMENT OF GLYCOSYLPHOSPHATIDYLINOSITOL

(57) Abstract: The invention relates to chimerical recombinant polypeptides, preferably therapeutic polypeptides, for example cytokines or antibodies, which are engineered to include a signal sequence for the attachment of glycosylphosphatidylinositol; cells expressing said polypeptides and methods to manufacture said polypeptides.

WO 2004/090135 A3

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB2004/001572

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/19 C12N15/62 C07K14/52 C07K19/00 A61K38/19
A61K39/395 C07K16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BENTING JUERGEN H ET AL: "N-glycans mediate the apical sorting of a GPI-anchored, raft-associated protein in Madin-Darby canine kidney cells" JOURNAL OF CELL BIOLOGY, vol. 146, no. 2, 26 July 1999 (1999-07-26), pages 313-320, XP002301129 ISSN: 0021-9525 abstract	1,2,6,7, 34-40
Y		3-5, 8-18, 25-33

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 October 2004	07.03.05

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mandl, B

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DA COSTA CLIVE R ET AL: "Production of the thyrotrophin receptor extracellular domain as a glycosylphosphatidylinositol-anchored membrane protein and its interaction with thyrotrophin and autoantibodies" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 19, 8 May 1998 (1998-05-08), pages 11874-11880, XP002246413 ISSN: 0021-9258 abstract figure 1	4,5
Y	WO 96/34105 A (FASEL NICOLAS JOSEPH ; REYMOND CHRISTOPHE DOMINIQUE (CH); RMF DICTAGEN) 31 October 1996 (1996-10-31) page 6, line 24 - line 31	3,30
Y	US 6 136 563 A (OLSON KENNETH ET AL) 24 October 2000 (2000-10-24) cited in the application column 4, line 17 - line 60	8-18
Y	WO 02/083851 A (GENVEC INC ; KESSLER PAUL D (US); KOVESDI IMRE (US)) 24 October 2002 (2002-10-24) paragraph '0096! - paragraph '0099!	25-33
Y	BROSTEDT P ET AL: "CHARACTERIZATION OF DIMERIC FORMS OF HUMAN PITUITARY GROWTH HORMONE BY BIOASSAY, RADIORECEPTOR ASSAY, AND RADIOIMMUNOASSAY" ACTA ENDOCRINOLOGICA, vol. 122, no. 2, 1 February 1990 (1990-02-01), pages 241-248, XP000618626 ISSN: 0001-5598 abstract; table 2	25-33
X	GUADIZ GAYLE ET AL: "The carboxyl terminus of Pneumocystis carinii glycoprotein A encodes a functional glycosylphosphatidylinositol signal sequence" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 40, 2 October 1998 (1998-10-02), pages 26202-26209, XP002301131 ISSN: 0021-9258 abstract	1,2,6,7, 34-39

-/--

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB2004/001572

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/017944 A (WAGNER THOMAS E ; WEI YANZHANG (US); GREENVILLE HOSPITAL SYSTEM (US)) 6 March 2003 (2003-03-06) page 3, line 2 – line 3 page 3, line 14 - line 16 page 3, line 23 - line 31 page 6, line 8 – line 24 page 8	1,2,6,7, 34-40
A	MEYERS R A (ED): "Molecular Biology and Biotechnology. A comprehensive desk reference , cytokines" MOLECULAR BIOLOGY AND BIOTECHNOLOGY: A COMPREHENSIVE DESK REFERENCE, 1995, pages 200-204,392, XP002246550 page 200 - page 204 page 392	1,2
A	WO 01/96565 A (ARTYMIUK PETER ; ASTERION LTD (GB); ROSS RICHARD (GB); SAYERS JON (GB)) 20 December 2001 (2001-12-20) page 8, line 14 - line 15 page 9, line 10 - line 21	25-33

INTERNATIONAL SEARCH REPORT

application No.
PCT/GB2004/001572

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 40 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-8 (partially), 9-18 (completely), 25-40 (partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8 (partially), 9-18 (completely), 25-40 (partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to growth hormone.

   ---

2. claims: 1-8, 25-40 (all partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to leptin.

   ---

3. claims: 1-8, 25-40 (all partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to erythropoietin.

   ---

4. claims: 1-8, 25-40 (all partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to prolactin.

   ---

5. claims: 1-8, 25-40 (all partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to TNF.

   ---

6. claims: 1-8, 25-40 (all partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to an interleukin.

   ---

7. claims: 1-8, 25-40 (all partially)

   Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to G-CSF.

   ---

8. claims: 1-8, 25-40 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to GM-CSF.

---

9. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to CNTF.

---

10. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to cardiotrophin-1.

---

11. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to LIF.

---

12. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to oncostatin M.

---

13. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to interferon.

---

14. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to a cytokine not covered by subjects 1-13.

---

15. claims: 1 (partially), 19-24 (completely), 25-40 (partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to an antibody.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

16. claims: 1-8, 25-40 (all partially)

Subject-matter relating to a chimeric polypeptide which is engineered to include a domain for attachment of at least one glycosylphosphatidylinositol molecule to a polypeptide which is not a ligand binding domain of a cytokine receptor and which is not covered by subjects 1-15.

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB2004/001572

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9634105	A	31-10-1996	US	6113917 A	05-09-2000
			AU	714808 B2	13-01-2000
			AU	5648196 A	18-11-1996
			BR	9604989 A	30-11-1999
			CA	2218987 A1	31-10-1996
			CZ	9703378 A3	15-04-1998
			WO	9634105 A1	31-10-1996
			EP	0826050 A1	04-03-1998
			HU	9802238 A2	28-01-1999
			JP	11504215 T	20-04-1999
			NL	1001348 C2	28-10-1996
			NO	974924 A	19-12-1997
			NZ	307195 A	29-07-1999
			NZ	335929 A	26-01-2001
			PL	323078 A1	02-03-1998
			ZA	9603269 A	25-10-1996
US 6136563	A	24-10-2000	US	5849535 A	15-12-1998
			US	5534617 A	09-07-1996
			US	6057292 A	02-05-2000
			US	6004931 A	21-12-1999
			AU	718439 B2	13-04-2000
			AU	7073396 A	09-04-1997
			CA	2230492 A1	27-03-1997
			DE	851925 T1	14-08-2003
			EP	0851925 A1	08-07-1998
			ES	2190388 T1	01-08-2003
			JP	11512298 T	26-10-1999
			WO	9711178 A1	27-03-1997
			ZA	9607973 A	23-06-1997
			US	6022711 A	08-02-2000
			US	6143523 A	07-11-2000
			US	5854026 A	29-12-1998
WO 02083851	A	24-10-2002	US	2003027751 A1	06-02-2003
			WO	02083851 A2	24-10-2002
WO 03017944	A	06-03-2003	CA	2458236 A1	06-03-2003
			EP	1427426 A2	16-06-2004
			WO	03017944 A2	06-03-2003
			US	2003105054 A1	05-06-2003
WO 0196565	A	20-12-2001	AU	7423401 A	24-12-2001
			CA	2447632 A1	20-12-2001
			EP	1290170 A2	12-03-2003
			WO	0196565 A2	20-12-2001
			JP	2004503243 T	05-02-2004
			US	2004071655 A1	15-04-2004